

## LIQUID MEDICINE INFUSION APPARATUS

### Field of the Invention

5     [0001]     The present invention relates to an infusion apparatus for administering a liquid medicine into a blood vessel, extradural cavity or hypodermically in small increments. Particularly, the invention relates to a liquid medicine infusion apparatus which can maintain a predetermined infusion rate stably for a long time  
10     without regard to the type of liquid medicine or the ambient temperature.

### Background of the Invention

15     [0002]     Among liquid medicines such as antibiotics and anti-cancer medicines and anesthetics, some liquid medicines are preferably administered into a blood vessel, extradural cavity or hypodermically little by little over a long time. Examples of known liquid medicine infusion apparatuses used for this purpose  
20     include a syringe pump type, in which the plunger of a syringe is pushed little by little by means such as a motor to thereby infuse the liquid medicine, and a roller pump type, in which a tube which is a conduit for a liquid medicine is slowly squeezed by a roller to force out the liquid medicine. Since these liquid medicine  
25     infusion apparatuses use electric power, they have an advantage that they can maintain an accurate infusion rate. However, because

these liquid medicine infusion apparatuses generate the power for forcing out the liquid medicine by using electric energy, when one of the apparatuses is used for a long time, a large-sized battery needs to be used. Therefore, the infusion apparatus itself becomes heavy, making it very inconvenient for a patient to carry the infusion apparatus. In addition, such liquid medicine infusion apparatuses are complicated in structure and thus are expensive.

[0003] In view of the above drawbacks, there have also been proposed liquid medicine infusion apparatuses which do not use electric power. For example, Japanese Patent Unexamined Publication No. 2-11160 discloses a liquid medicine infusion apparatus in which a flow rate control unit composed of a tube having a small inner diameter is connected to liquid medicine pressurizing/supplying means such as a balloon. In this liquid medicine infusion apparatus, the infusion rate of a liquid medicine forced out from the balloon is controlled to a predetermined constant value due to the line resistance of the small-diameter tube while the liquid medicine passes through the flow rate control unit consisting of the small-diameter tube.

[0004] However, the control of the flow rate achieved by making use of the line resistance of the small-diameter tube is greatly influenced by the viscosity of the liquid medicine. That is, since the flow rate  $F$  of the liquid medicine after it passes through the small-diameter tube follows the Hagen-Poiseuille's law (see the

following equation 1), it is in inverse proportion to the viscosity  $\eta$  of the liquid medicine.

$$F = \frac{gP\pi(d/2)^4}{8\eta l} \quad (1)$$

- 5     F: flow rate of liquid medicine (cm<sup>3</sup>/sec)  
      g: gravitational acceleration (980 cm/s)  
      P: pressure applied to liquid medicine (kPa)  
      d: inner diameter of small-diameter tube (cm)  
       $\eta$ : viscosity of liquid medicine (g/cm·s)  
10    l: length of small-diameter tube (cm)  
       $\pi$ : ratio of circumference of circle to its diameter

[0005]     Meanwhile, the viscosity of a liquid medicine becomes lower as the temperature rises according to the general properties  
15    of a fluid. Therefore, the flow rate of the liquid medicine increases in inverse proportion to the rise in the temperature of the liquid medicine. For example, the viscosity at 25°C of fluorouracil which is an anti-malignant antineoplastic agent is 1.273 g/cm·s whereas its viscosity at 32°C is reduced to 1.084  
20    g/cm·s. Therefore, the flow rate at 32°C of fluorouracil is about 17.4% higher than that at 25°C.

[0006]     The viscosity of a liquid medicine differs according to

the type of the liquid medicine as well. For example, the viscosity at 25°C of fluorouracil is 1.273 g/cm·s whereas the viscosity at 25°C of cisplatin which is an anti-malignant tumor platinum complex is 0.898 g/cm·s. Therefore, the flow rate of a liquid medicine varies according to the type of the liquid medicine as well.

[0007] Thus, a liquid medicine infusion apparatus having a flow rate control unit, which consists of a small-diameter tube, connected to liquid medicine pressurizing/supplying means has a drawback in that a predetermined constant infusion rate cannot be obtained when the viscosity of a liquid medicine changes according to the type and temperature of the liquid medicine.

[0008] Therefore, conventionally known liquid medicine infusion apparatuses cannot be used for a long time without a large-sized battery or the liquid medicine infusion rate thereof is affected by the type and temperature of the liquid medicine.

[0009] It is an object of the present invention, which has been made in view of the current state of the prior art, to provide a liquid medicine infusion apparatus which does not have the drawbacks of conventionally known liquid medicine infusion apparatuses. Stated more specifically, it is an object of the present invention to provide a liquid medicine infusion apparatus which can be used for a long time without using a large-sized

battery and can infuse a liquid medicine stably by maintaining a predetermined constant infusion rate without regard to the type and temperature of the liquid medicine.

5     Summary of the Invention

10     [0010]     The inventors of the present invention have conducted intensive studies to solve the above problems and have found that the above problems can be solved by controlling the flow rate in a liquid medicine infusion apparatus which includes a liquid medicine pressurizing/supplying means and a flow rate control unit connected to the liquid medicine pressurizing/supplying means with a novel mechanism that does not use a small-diameter tube as a flow rate control unit. The present invention has been accomplished based on this finding.

[0011]     That is, the present invention relates to a liquid medicine infusion apparatus characterized by including the following means (a) to (e):

20             (a) liquid medicine pressurizing/supplying means;

             (b) a secondary pressurizing means which is connected in liquid communication with the liquid medicine pressurizing/supplying means by an upstream passage;

25             (c) upstream opening/closing means arranged in the upstream passage, for opening and closing the liquid communication state between the liquid medicine pressurizing/supplying means and the

secondary pressurizing means;

(d) downstream opening/closing means arranged in a downstream passage provided downstream of the secondary pressurizing means; and

5 (e) control means for controlling the opening/closing timings of the upstream opening/closing means and of the downstream opening/closing means.

[0012] According to another preferred embodiment of the present  
10 invention, the pressurizing means of the liquid medicine pressurizing/supplying means is a rubber elastic body, a spring, or air pressure.

[0013] According to still another preferred embodiment of the  
15 present invention, the pressurizing means of the secondary pressurizing means is a rubber elastic body, a spring, or air pressure.

[0014] According to yet still another preferred embodiment of  
20 the present invention, the upstream opening/closing means and the downstream opening/closing means are comprised of electromagnetic valves, clamps, or an integrated unit using a stopcock.

#### Brief description of the Drawings

25 [0015] Fig. 1 is a schematic diagram of a liquid medicine

infusion apparatus according to one embodiment of the present invention.

Figs. 2 (a) to (e) are diagrams for explaining the liquid medicine infusing operation of the liquid medicine infusion apparatus shown in Fig. 1.

Fig. 3 is a schematic diagram of a liquid medicine infusion apparatus according to another embodiment of the present invention.

Fig. 4 is a schematic diagram of a liquid medicine infusion apparatus according to still another embodiment of the present invention.

Fig. 5 is a schematic diagram of a liquid medicine infusion apparatus according to yet still another embodiment of the present invention.

Fig. 6 is a schematic diagram of a flow rate control unit of the liquid medicine infusion apparatus shown in Fig. 5 as viewed from above.

Fig. 7 is a schematic diagram of a liquid medicine infusion apparatus according to further still another embodiment of the present invention.

Figs. 8 (a) to (d) are diagrams for explaining the liquid medicine infusing operation of the liquid medicine infusion apparatus shown in Fig. 7.

#### Preferred Embodiments of the Invention

[0016] The liquid medicine infusion apparatus of the present

invention will be described with reference to the accompanying drawings. However, the present invention is not limited to the embodiments shown in the drawings, but instead includes all embodiments within the scope and spirit of the appended claims.

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[0017] Fig. 1 is a schematic diagram of a liquid medicine infusion apparatus according to one embodiment of the present invention. The liquid medicine infusion apparatus of Fig. 1 includes liquid medicine pressurizing/supplying means 1, secondary  
10 pressurizing means 5, upstream opening/closing means 3, downstream opening/closing means 4, and control means 7 for controlling the opening/closing timing of the upstream opening/closing means and of the downstream opening/closing means. In the embodiment shown in Fig. 1, the liquid medicine pressurizing/supplying means 1 and the  
15 secondary pressurizing means 5 are connected to each other by an upstream passage 2 and a downstream passage 6 is provided downstream of the secondary pressurizing means 5.

[0018] In the liquid medicine infusion apparatus of the present  
20 invention, the liquid medicine pressurizing/supplying means 1 stores a liquid medicine and forces out the liquid medicine toward the secondary pressurizing means 5 by pressurization to cause a flow of the liquid medicine. As the liquid medicine  
pressurizing/supplying means 1, there may be used a balloon which  
25 makes use of the shrinkage force of a rubber elastic body. The liquid medicine is stored inside of the expanded balloon. The



balloon is shrunk by natural force of the rubber elastic body. A syringe which makes use of the resilient pressure of a spring is also used as the liquid medicine pressurizing/supplying means 1. The liquid medicine is stored inside of the syringe and forced out of the syringe using a plunger having a resilient spring. A pressure bag which makes use of air pressure is also used. The pressure bag is made of a flexible plastic film contained in a rigid container. The liquid medicine is stored in the bag and is forced out of the bag using air introduced into the rigid container to press the bag. A means that mechanically pressurizes a bag filled with liquid medicine by a pump, such as an infusion pump, is also used. As for the pressurization of the liquid medicine by the liquid medicine pressurizing/supplying means 1, a pressure of 50 to 100 kPa is desirably applied to the liquid medicine to force it out toward the secondary pressurizing means 5.

[0019] In the liquid medicine infusion apparatus of the present invention, the secondary pressurizing means 5 is connected in liquid communication with the liquid medicine pressurizing/supplying means 1 by the upstream passage 2. The secondary pressurizing means 5 temporarily stores the liquid medicine supplied from the liquid medicine pressurizing/supplying means 1, and forces it out through downstream passage 6 by pressure. The upstream passage 2 and downstream passage 6 are each typically a thermoplastic tubing made of polyvinyl chloride, polyethylene, polybutadiene, silicone and the like. The upstream

passage 2 and downstream passage 6 are sized so as not to restrict the flow of the liquid medicine therethrough and, for example, are tubing having an inner diameter of from about 0.5 mm to about 5 mm.

5 [0020] The secondary pressurizing means 5 has a very small capacity as compared to the pressurizing/supplying means 1 and is sized so as to receive (from the pressurizing/supplying means 1) and discharge (into the downstream passage 6) small increments, or doses, e.g., 0.05 ml, of the liquid medicine. As shown in Fig. 1  
10 the secondary pressurizing means 5 consists of a spring 51, a gasket 52, and a cylinder 53, and generates internal pressure by making use of the elastic force of the spring. Other examples of the secondary pressurizing means include those which generate internal pressure by using a plastic sheet 54 such as a vinyl  
15 chloride, silicone rubber, or thermoplastic elastomer sheet in place of the gasket and pressing it by the spring 51 as shown in Fig. 3 and those using a rubber elastic balloon as shown in Fig. 4. However, the present invention is not limited to these means. The pressure (internal pressure) of the secondary pressurizing means 5  
20 is generally set to a value 10 to 20% lower than the pressure of the liquid medicine pressurizing/supplying means 1. Therefore, the liquid medicine can flow from the liquid medicine pressurizing/supplying means 1 to the secondary pressurizing means 5.

25 [0021] In the liquid medicine infusion apparatus of the present

invention, the upstream opening/closing means 3 is arranged in the upstream passage 2 to open or close the liquid communication between the liquid medicine pressurizing/supplying means 1 and the secondary pressurizing means 5. In the liquid medicine infusion apparatus of the present invention, the downstream opening/closing means 4 is arranged in the downstream passage 6 provided downstream of the secondary pressurizing means 5 to open or close the liquid communication between the secondary pressurizing means 5 and the downstream passage 6. It is preferred that the upstream opening/closing means 3 and the downstream opening/closing means 4 can be opened/closed with an operational force as small as possible to allow its usage for a long time. The upstream opening/closing means 3 and the downstream opening/closing means 4 are not necessarily separate units and can be integrated into a single unit capable of performing the functions of both means. The upstream opening/closing means 3 and the downstream opening/closing means 4 shown in Fig. 1 are electromagnetic valves. Other examples of the upstream opening/closing means 3 and the downstream opening/closing means 4 include clamps for clamping a tube used as the liquid medicine passage from outside to close the passage at predetermined time intervals by making use of the rotation of a motor 8 shown in Figs. 5 and 6, and an integrated unit obtained by integrating the upstream opening/closing means 3 and the downstream opening/closing means 4 by making use of a stopcock 9 shown in Figs. 7 and 8. However, the present invention is not limited to these means.

[0022] In the liquid medicine infusion apparatus of the present invention, the control means 7 serves to control the opening/closing timing of the upstream opening/closing means 3 and of the downstream opening/closing means 4. The control of the opening/closing timing of these opening/closing means makes it possible to attain a predetermined liquid medicine infusion rate in the liquid medicine infusion apparatus of the present invention.

[0023] A description is subsequently given of the liquid medicine infusing operation of the liquid medicine infusion apparatus according to the embodiment of the present invention shown in Fig. 1 with reference to Figs. 2(a) to 2(f).

[0024] As described above, the liquid medicine infusion apparatus of the present invention infuses a liquid medicine by controlling the opening/closing timing of the upstream opening/closing means 3 and of the downstream opening/closing means 4 by the control means 7.

[0025] When the liquid medicine infusion operation is started while the upstream opening/closing means 3 is opened and the downstream opening/closing means 4 is closed (Fig. 2(a)), because the pressure (internal pressure) of the secondary pressurizing means 5 is set to a value lower than the pressure of the liquid medicine pressurizing/supplying means 1, the liquid medicine flows into the secondary pressurizing means 5 from the liquid medicine

pressurizing/supplying means 1 and is stored in the secondary  
pressurizing means 5. Since the capacity of the secondary  
pressurizing means 5 is very small, the liquid medicine from the  
liquid medicine pressurizing/supplying means 1 is filled into the  
5 secondary pressurizing means 5 substantially instantaneously after  
the start of the liquid medicine infusing operation, and the state  
shown in Fig. 2(b) is obtained.

[0026] When the filling of the liquid medicine into the  
10 secondary pressurizing means 5 is completed, the upstream  
opening/closing means 3 is closed, and a state shown in Fig. 2(c)  
is obtained.

[0027] Next, when the downstream opening/closing means 4 is  
15 opened (Fig. 2(d)), the liquid medicine stored in the secondary  
pressurizing means 5 is forced out by the pressure (internal  
pressure) of the secondary pressurizing means 5 and supplied to a  
patient through the downstream passage 6. Since the capacity of  
the secondary pressurizing means 5 is sufficiently small and the  
20 pressure of the secondary pressurizing means 5 is applied to the  
liquid medicine, the liquid medicine stored in the secondary  
pressurizing means 5 is completely discharged into the downstream  
passage 6 substantially instantaneously upon opening of the  
downstream opening/closing means 4, and the state shown in Fig.  
25 2(e) is obtained.

[0028] When the discharge of the liquid medicine from the secondary pressurizing means 5 is completed, the downstream opening/closing means 4 is closed, and the state shown in Fig. 2(f) is obtained.

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[0029] Figs. 8(a) to 8(d)) illustrate a liquid medicine infusion operation using the liquid medicine infusion apparatus shown in Fig. 7. The liquid medicine infusion apparatus shown in Fig. 7 includes a stopcock 9 which performs the functions of both the upstream opening/closing means and the downstream opening/closing means. Figs. 8(a) and 8(b) show the stopcock 9 simultaneously open to upsteam passage 2 and closed to downstream passage 6 such that liquid medicine flows into the secondary pressurizing means 5 from the liquid medicine pressurizing/supplying means 1 and is stored in the secondary pressurizing means 5. In Figs. 8(c) and 8(d), the stopcock 9 is closed to upsteam passage 2 and open to downstream passage 6 such that liquid medicine is forced out of the secondary pressurizing means 5 through downstream passage 6.

[0030] The above operation of dosing a patient with the liquid medicine little by little (i.e., intermittently in small increments) is repeated so that the liquid medicine infusion apparatus of the present invention can infuse the liquid medicine stably while maintaining a fixed infusion rate. For example, when the inner capacity of the secondary pressurizing means 5 is 0.05 ml and the liquid medicine infusion operation is repeated once a

minute, 0.05 ml per minute or 3 ml per hour of a liquid medicine is dosed to a patient. Even when the inner capacity of the secondary pressurizing means 5 is 0.05 ml, by repeating the liquid medicine infusion operation twice a minute, 0.1 ml per minute or 6 ml per hour of a liquid medicine is dosed to a patient.

[0031] Therefore, in the liquid medicine infusion apparatus of the present invention, the liquid medicine infusion rate (dose of the liquid medicine to a patient per unit time) can be controlled by adjusting the opening/closing timing of the upstream opening/closing means and of the downstream opening/closing means by the control means.

[0032] Thus, the liquid medicine infusion apparatus of the present invention has an advantage in that a predetermined fixed infusion rate can be maintained even when the viscosity of a liquid medicine changes due to a change in the type or temperature of the liquid medicine because it controls the liquid medicine infusion rate (flow rate) without making use of the line resistance of a small-diameter tube, unlike conventional liquid medicine infusion apparatus in which liquid medicine pressurizing/supplying means such as a balloon is connected to a flow control unit composed of a tube having a small inner diameter. In addition, unlike conventional liquid medicine infusion apparatuses which generate power for forcing out a liquid medicine by using electric energy, the liquid medicine infusion apparatus of the present invention

requires no electric energy, or even if it does, it requires only the electric energy necessary for the control means to open or close the upstream opening/closing means and the downstream opening/closing means. Therefore, the liquid medicine infusion apparatus of the present invention does not require a large battery even when it is used for a long time, thereby making it possible to reduce the weight of a pump itself. Accordingly, the liquid medicine infusion apparatus of the present invention has advantages in that it can be conveniently carried by a patient and its cost can be reduced.